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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,038	07/10/2000	Antonio J. Grillo-Lopez	P1752R1	9334

7590 07/28/2004

Attn Wendy Lee
1 DNA Way
South San Francisco, CA 94080-4990

EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	09/613,038	GRILLO-LOPEZ ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-16,22,28 and 32-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-16,22,28 and 32-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/16/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 6/16/04, is acknowledged.

2. Claims 1, 5-16, 22, 28 and 32-42 are pending and under examination in this application.

3. In view of the amendment filed on 6/16/04, only the following rejection are remained.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 10, 32 and 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the hybridoma that produce the 2B8 antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the hybridoma, which produces this antibody, may satisfy first paragraph. See 37 CFR 1.801-1.809.

If the deposits have been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridoma has been deposited under the Budapest Treaty and that the hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample *or for the enforceable life of the patent whichever is longer*. See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Applicant argues that the 2B8 antibody is a murine antibody produced by a hybridoma that was deposited under the Budapest treaty on June 22, 1993 with the Type Culture Collection under deposit number HB11388. Applicant draws the Examiner's attention to U.S. Patent N.

5,736,137 for the deposited antibody 2B8. However, the `137 patent did not fulfill the Biological deposit of the antibody 2B8. The Examiner notices that the `137 patent only fulfill the Deposit material for the chimeric anti-CD20 antibody, ATCC deposit number 69119.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 5-6, 11-16, 22, 28, 34-39 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/04281 (IDS Ref. No. 31).

The `281 publication teaches and claims an improved method of treating immune cell mediated diseases comprising administering a therapeutic protein such as a monoclonal antibody (see published claim 1), wherein the immune cell is a B-cell (see published claim 19), wherein the B-cell antigen is human CD20 (see published claim 23), wherein the therapeutic protein is a monoclonal antibody to human CD20 (see published claim 25),, wherein the dose is given intravenously (published claim 15) and wherein the B-cell mediated disease is graft verses host disease (see published claim 21 in particular). The `281 publication further teaches that the therapeutic proteins are useful in the treatment of transplanted organ rejection such as heart, lung, kidney, cornea, bone marrow, skin, etc (see page 10 lines 1-3 in particular). In addition, the `281 publication teaches that the monoclonal antibody can be chimeric, human or humanized (see page 7, lines 5-14 in particular). The `281 publication teaches that the administration can be accomplished subcutaneous (see page 7, under Route of Administration) or intravenously (see page 1 line 14-15, page 20, under intravenous administration and tables 1-5). The `281 publication further teaches a dosing regimen of 10mg/kg (see page 3, line 18) or 40, 80, 100, 120, 140 mg/bi-week (see page 10, lines 30-3 and tables 1-5). The `281 publication teaches that the improvement method comprises administering a dose of therapeutic protein (i.e. anti-CD20), followed by a second administration of said therapeutic protein, wherein the systemic exposure of said therapeutic protein from the second administration is at least 50% greater than the systemic exposure from a first (see published claim 1). The `281 publication teaches prophylatic use in transplanted organ rejection (see page 10, lines 13-14 in particular).

Claims 13-15 are included because the specific doses taught by the '281 publication anticipate the claimed rages.

Claim 22 is included because the `281 publication teaches a prophylatic use in transplanted organ rejection, therefore it will be immediately apparent to administer the antibody to the mammal before the mammal is exposed to the graft in the prophylatic use of the transplanted organ rejection.

The reference teachings anticipate the claimed invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 7-10, 28, 32, 40 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/04281 (IDS Ref. No. 31) in view of Business Wire (2/24/1998).

The teachings of WO 98/04281 publication have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that the antibody comprises rituximab in claims 7 and 40, conjugated with a cytotoxic agent in claim 8, Y2B8 in claims 10, 32, and 41 wherein the cytotoxic agent is a radioactive compound in claim 9.

The Business Wire article teaches IDEC-Y2B8, Rituxan™ (Rituximab), is a monoclonal antibody tightly conjugated to the radioisotope yttrium-90, which targets the CD20 antigen on mature normal and malignant B cells. Further the article teaches that the MX-DTPA used to create IDEC-Y2B8 exhibits excellent in vivo retention of yttrium. Further, studies in mice have shown minimal loss of the radioisotope from the conjugate and not significant accumulation of yttrim in bone. The article further teaches that IDEC Pharmaceuticals focuses on developing targeted therapies for the treatment of cancer and autoimmune diseases, IDEC's antibody products act chiefly through immune system mechanisms, exerting their effect by binding to specific, readily targeted immune cells in the patient's blood or lymphatic systems (see the entire article).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the monoclonal antibody to human CD20 taught by the `281 publication with the Y2B8 antibody as taught by the Business Wire article.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because IDEC-Y2B8 exhibits excellent in vivo retention of yttrium as taught by Business Wire article.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. Claims 1, 8-10, 28, 33 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/04281 (IDS Ref. No. 31) in view of U.S. Pat. No. 6,498,181.

The teachings of WO 98/04281 publication have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that the antibody is conjugated with a cytotoxic agent in claim 8, ^{131}I-B1 in claims 10, 33, and 42 wherein the cytotoxic agent is a radioactive compound in claim 9.

The `181 patent teaches ^{131}I labeled anti-B1 (Bexxar) mAb, raised to the CD-20 antigens that are expressed on the surface of mature B-cells, is one example of a radiolabeled mAb that has seen successful in treating follicular non-Hodgkins lymphoma in recent clinical trials (see co. 9, lines 19-30 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the monoclonal antibody to human CD20 taught by the `281 publication with the $^{131}$I-B1 antibody as taught by the `181 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because ^{131}I-B1 has seen successful in recent clinical trials as taught by `181 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
July 22, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600